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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,604	MCLACHLAN ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *1-8,19-31 and 34-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *9-18,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/10/04, 1/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: Exhibit A

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II (claims 89-18 and 32-33) with SEQ ID NO: 2 in the reply filed on 1/20/06 is acknowledged.

Applicants argue that the Examiner has not shown a serious burden of examining all the groups together. These have been considered, but not found persuasive. As discussed in the prior Office Action (election requirement, 10/20/05), first, Groups I, III, IV, VI, IX, XI, and XII are drawn to structurally and functionally different products, which have different classification. The search required for one group is not required for the other Groups because each group requires a different non-patent literature search, such as sequence search, due to each group comprising different products. Therefore, restriction for examination purposes as indicated is proper. Secondly, Groups II, V, VII, VIII and X are unrelated method because each invention has different method objectives and different modes of operations. Therefore, each invention may need different patient population or biological samples from different patients. Invention II, III, or X are methods for treating cancer patient or precancer patients with different materials, antibody (II) or polypeptide (III) or DNA as vaccine (X). Inventions VII or VIII are method for in vitro detecting expression of IGSF or LIV-1 using antibody (VIII) or using a polypeptide (VII). Searching these groups together would impose a serous burden because each group has acquired a separate status in the art as shown by their different classification, and the search required for one group is not required for the other groups because each group requires a different non-patent literature search due to each group comprising different products and/or method steps, Therefore, restriction for examination purposes as indicated is proper. In addition, Applicants argue that the composition and method should be examined with antibody group. In response to this argument, the claimed compositions comprising intent use for cancer treatment, therefore, at this time they are combined with the method of treating cancer for examination. For the reasons discussed above, the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made **FINAL**.

Claims 1-43 are pending. Claims 1-8, 19-31 and 34-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Claims 9-18, 32-33 will be examined on the merits.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 11/10/04 and 1/20/06 are/is considered by the examiner and initialed copies of the PTO-1449 are enclosed.

Claim Rejections - 35 USC § 112

The following is a quotation of the **second paragraph of 35 U.S.C. 112**:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 12-18 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 12-18 are vague and indefinite because the term "associates with IGSF9" in the claims 9 and 12 is not clear. It cannot be determined what the meaning of "associates with IGSF9" is. Does it mean to bind to IGSF9 protein or not? Therefore, the metes and bounds of the claims cannot be determined. Furthermore, claims 9 and 12 also render the dependent claims 32 and 13-18 indefinite.

The following is a quotation of the **first paragraph of 35 U.S.C. 112:**

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-18 and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are drawn to a composition and method of treating a mammal exhibiting a neoplastic disorder comprising administering an antibody or antigen binding fragment that is associated with IGSF9 (referred as SEQ ID NO: 2, page 7 of instant specification or para 30). To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provide an enabling disclosure of how to make and use a claimed invention. The method objective of claims is a method of treating a cancer with antigen binding fragment comprising an antibody to IGSF9. Thus, it would be expected that one of skill in the art would be able to treat a neoplastic disorder comprising a cancer with any antibody to IGSF9 without undue experimentation by using the claimed method.

The specification teaches a method of generating a monoclonal anti-IGSF9 antibody (see pages 93-94). The specification teaches a general method of treating cancer and states that based on analysis of the levels of IGSF9 in tumor sample a treatment regime is determined using acceptable treatment alternative known to those skilled in the art. However, the specification does not provide a method of treating any cancer with any agent, which could bind to IGSF9 comprising an antibody to IGSF9 (SEQ ID NO: 2). Thus, the specification invites the skilled artisan to experiment to determine how to use the claimed antibody or binding fragment to IGSF9 and does not set forth sufficient teachings to allow one skilled in the art to practice treating a neoplastic disorder including a cancer. There are no working examples to guide or assist the skilled artisan in practicing the claimed method of treating any neoplastic disorder with antibody or binding fragment to IGSF9.

The instant specification provides insufficient guidance or direction to predictably enable one of ordinary skill in the art to use the invention as claimed. Those of skill in the art recognize the unpredictability of treating tumors with antibodies. For example, Jain R. K. (Scientific American, 271(1): 58-65, July 1994) discloses the art known barriers to the delivery of drugs into solid tumors. These impediments include (1) Non-uniform blood delivery to all areas of the tumor in which some areas of the tumor receive therapeutic agents and other areas of the tumor receive no therapeutic agent at all. (Page 60 col. 3); (2) Increased viscosity of blood in the tumor itself which also hinders drug delivery to the tumor (see paragraph bridging pages 60 and 61); (3) High liquid pressures in the interstitial matrix can retard the delivery of large therapeutic agents, such as antibodies, into tumors (page 61, Col. 1 paragraph 1); (4) Convection is a necessary mechanism by which larger therapeutic molecules such as antibodies, reach target cells which are not directly fed by the vasculature. Convection is not observed in large tumors (defined as more than ½ centimeter in diameter, page 62 col. 1) and convection is necessary for adequate drug delivery of molecules having a molecular weight of more than 5000 (page 61, col. 1 through page 63, col. 3) and (4) Molecules as large as antibodies (i.e., MW=150,000) would require several months to reach a uniform concentration in a tumor that measures 1 centimeter in radius (page 63, col. 2). Further, Dillman R. O., (Annals of Internal Medicine, 111:592-603, 1989) summarizes (see abstract) the status of in-vivo use of monoclonal antibodies for treating cancer wherein despite advances in biotechnology, many major hurdles persist including tumor cell heterogeneity, lack of cytotoxicity, and the development of human anti-mouse antibodies (HAMA). Also, Weiner L. M. (Seminars in Oncology, 26 (4 Suppl 12): 41-50, August 1999) provided an overview of monoclonal antibody therapy including some promising activity, however, major obstacles to clinical efficacy still exist extending the unpredictability of this treatment. This includes impaired distribution and delivery of antibody to the tumor site, inadequate trafficking of potential cellular effectors to tumor, antigenic heterogeneity, shed or internalized targets and insufficient target specificity (see page 43).

Furthermore, as disclosed by Dillman, R. O.(Journal of Clinical Oncology, 12(7):1497-1515, 1994) discloses, after reviewing the literature on the use of unconjugated monoclonal antibodies to treat cancer, that "at present, there are no unconjugated monoclonal antibodies that have proven therapeutic benefit in

hematologic malignancies or solid tumors." Thus, absent objective evidence to the contrary, it is highly unpredictable that applicant's unconjugated antibody would possess any therapeutic effects.

Baughn et al (WO2003051902, filed 5/31/02) teach that a protein, which is 100% identical to the amino acid sequence of SEQ IDNO: 2 (referred to IGSF9, instant specification, page 7 or para 30) is neurotransmitter (see abstract and exhibit A). Thus, absent objective evidence to the contrary, it is highly unpredictable that claimed binding fragment or antibodies that bind IGSF9 would possess any therapeutic effect for just any neoplastic disorder comprising cancer.

No direction or guidance is provided in current specification to assist one skilled in the art using a binding fragment or antibody that binds IGSF9 (SEQ ID NO:2) in a method of treating neoplastic disorder in a mammal. In view of the lack of the predictability of the art to which the invention pertains as evidenced by the art of Jain R. K., Dillman R. O. (Weiner L. M., Dillman J., Satyamoorthy et al and Lehmann et al, and the lack of established clinical protocols for effective immunotherapy, one skilled in the art would be forced into under experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-18 and 32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoefnagel et al., (Eur J Nucl Med, vol 28, page 359-68, 2001).

Hoefnagel et al., teach a method of treating neuroblastoma in mice with an antibody to an immunoglobulin superfamily member L1-CAM (abstract) expressed in the brain tissue. Hoefnagel et al., also disclose that the anti-L1-CAM antibody, mAB chCE7, is Iodine-131 labeled and the antibody specifically binds to brain tissue, not other tissue such as kidney. Hoefnagel et al., further disclose that

the tumors were treated with single injection of 131I-mAB chCE7 and after the therapy the subcutaneous tumors nearly disappeared (abstract).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Dowining for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY

SHEELA HUFF
PRIMARY EXAMINER